PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

28 DEC 2004

To:

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Received with Thanks
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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	28.09.2004
Applicant's or agent's file reference: SUVN-RK-003	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IN 03/00222	19.06.2003	21.06.2002

Applicant
SUVEN LIFE SCIENCES LTD. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
SUVN-RK-003		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IN 03/00222	19.06.2003	21.06.2002
International Patent Classification (IPC) or both national classification and IPC		
C07D513/04		
Applicant		
SUVEN LIFE SCIENCES LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.01.2004	28.09.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Grassi, D Telephone No. +49 89 2399-8499

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IN 03/00222

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-51	as originally filed

Claims, Numbers

1-20, 21 (part)	as originally filed
21 (part), 22-27	received on 17.05.2004 with letter of 12.05.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IN 03/00222

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1(part),6,8-13,15-18

because:

☒ the said international application, or the said claims Nos. 6,8-13,15-18(with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1(part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-5,7,14,19-27
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

The claim 1 was only partly searched (cf. International Search Report, continuation of Box I.2).

Claims relating to inventions in respect of which no International Search Report has been established need not to be subject of the Written Opinion of the International Searching Authority (Rule 43bis.1(b) PCT in combination with Rule 66.1(e) PCT). Therefore, only the searched part of the present claims 1 is examined (compounds of Formula (I) but not its derivatives or analogs).

Claims 6, 8-13 and 15-18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

The amendments appear to be in conformity with Art. 34(2)b) PCT.

1) Reference is made to the following documents:
D1: Russell et al., Journal Of Medicinal Chemistry, 2001, 44(23), 3881-3895

2) The subject-matter of present claims 1-27 is new (Article 33(2) PCT).

3) The subject-matter of claims 1-27 does not involve an inventive step (Article 33(3) PCT).

The most relevant state of the art is represented by D1 disclosing 5-HT6 receptor ligands (cf. Table 1).

The technical problem underlying the present application is seen in the provision of alternative 5-HT receptor ligands.

D1 does not prompt the skilled in the art to the present compounds.

However, the present application appears not to contain any test data showing the activity of the claimed compounds. Consequently, it can be decided whether the

technical problem is solved or not and inventive activity of claim 1 cannot be assessed.
The claims relating composition comprising the compounds of claim 1 and the use thereof would only involve an inventive step if the claim 1 fulfilled the said requirement (claims 3-18).
The claims relating to the preparation of the compounds of claim 1, to the intermediates thereof and to the preparation of the intermediates would only involve an inventive step if the claim 1 fulfilled the said requirement (claims 19-27).

Further remarks
The terms *derivatives* or *analogs* are not clear (cf. claims 1, 3 and 14).

The claims 14, 19, 22, 25 and 27, referring only to a generic formula, should also refer to the claim where the said generic formula is defined.
In claim 27 the meaning of X is not specified.

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are as defined above, with formaldehyde and a compound of formula (V) given below,

$NHR_{13}R_{14}$

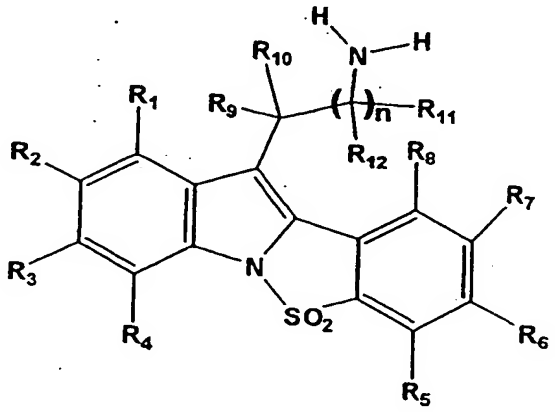
(V)

wherein R_{13} and R_{14} are as defined above.

22. A process for the preparation of compound of formula (I), which comprises of either chemically or catalytically reducing compounds containing =C(O) group/s in the side chain, to the corresponding –C(OH,H) or –C(H,H) compound.

23. A process according to Claim-19 to Claim-22, comprising of carrying out one or more of the following optional steps: i) removing any protecting group; ii) resolving the racemic mixture into pure enantiomers by the known methods and iii) preparing a pharmaceutically acceptable salt of a compound of formula (I) and/or iv preparing a pharmaceutically acceptable prodrug thereof.

24. Novel intermediates of general formula (III) are represented as given below,



(III)

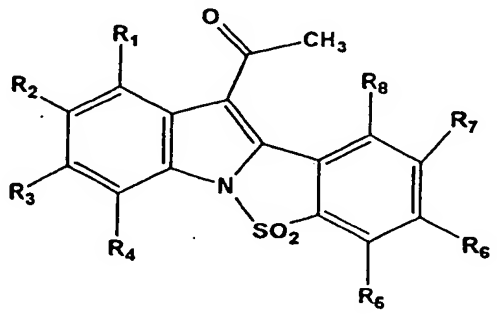
wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11} and R_{12} may be same or different and each independently represent hydrogen, halogen, oxo, thio, perhaloalkyl, hydroxy, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups such as linear or branched $(C_1$-$C_{12})$alkyl, $(C_2$-$C_{12})$alkenyl, $(C_2$-$C_{12})$alkynyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_7)$cycloalkenyl, bicycloalkyl, bicycloalkenyl, $(C_1$-$C_{12})$alkoxy, cyclo$(C_3$-$C_7)$alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino,

dialkylamino, arylamino, diarylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocyclylalkoxycarbonyl, heteroaryloxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acids and its derivatives, phosphoric acid and its derivatives; or the adjacent groups like R_1 and R_2 or R_2 and R_3 or R_3 and R_4 or R_5 and R_6 or R_6 and R_7 or R_7 and R_8 together with carbon atoms to which they are attached may form a 5, 6, or 7 membered ring, which may further optionally contain one or more double bonds and/or one or more heteroatoms such as the group "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms; or R_9 and R_{10} or R_{11} and R_{12} together represent double bond attached to "Oxygen" or "Sulfur"; or R_9 and R_{10} or R_{11} and R_{12} together with the carbon atoms to which they are attached may form a 3, 4, 5, or 6 membered ring, which may further optionally contain one or more double bonds, and/or one or more heteroatoms such as the group "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and also includes combination of one or more double bonds with "heteroatoms", as above defined.

"n" is an integer ranging from 1 to 8. It is preferred that n be 1 to 4. The carbon chains which "n" represents may be either linear or branched.

25. A process provided for the preparation of novel intermediate of the general formula (III) which comprises of cyclizing a suitable compounds of formula (II).

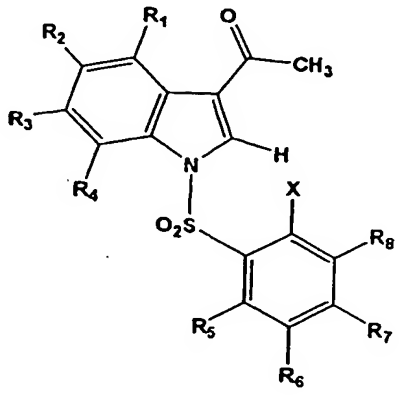
26. Novel intermediates defined of general formula (IV),



(IV)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are as may be same or different and each independently represent hydrogen, halogen, oxo, thio, perhaloalkyl, hydroxy, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups such as linear or branched (C_1-C_{12})alkyl, (C_2-C_{12})alkenyl, (C_2-C_{12})alkynyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12})alkoxy, cyclo(C_3-C_7)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, diarylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocyclylalkoxycarbonyl, heteroaryloxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acids and its derivatives, phosphoric acid and its derivatives; or the adjacent groups like R_1 and R_2 or R_2 and R_3 or R_3 and R_4 or R_5 and R_6 or R_6 and R_7 or R_7 and R_8 together with carbon atoms to which they are attached may form a 5, 6, or 7 membered ring, which may further optionally contain one or more double bonds and/or one or more heteroatoms such as the group "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms; and R_9 and R_{10} here are represented as double bond attached to "Oxygen".

27. A process provided for the preparation of novel intermediate of the general formula (IV) which comprises of cyclizing compounds of formula (VIII)



wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are as defined above; using a Pd(0) or Pd (II) derivative as a catalyst.